

WHAT IS CLAIMED IS:

- 1 1. A method for diagnosing a genetically transmitted glycosylation
2 disorder in a mammal, the method comprising:
3 a) providing a sample from a mammal, wherein the sample comprises
4 a plurality of glycoconjugates;
5 b) contacting the sample with either or both of:
6 a first type of diagnostic reagent that binds to a glycoconjugate
7 that has an oligosaccharide determinant that: i) is present on
8 glycoconjugates in a sample obtained from a mammal that has the
9 glycosylation disorder, and ii) is not present on glycoconjugates in a
10 sample obtained from a mammal that does not have the
11 glycosylation disorder; and
12 a second type of diagnostic reagent that binds to a
13 glycoconjugate that has an oligosaccharide determinant that is: i) is
14 present on glycoconjugates in a sample obtained from a mammal
15 that does not have the glycosylation disorder, and ii) is not present
16 on glycoconjugates in a sample obtained from a mammal that has
17 the glycosylation disorder; and
18 c) determining whether the diagnostic reagent binds to the
19 glycoconjugates in the sample, wherein the binding of a diagnostic reagent of the first type,
20 or the absence of binding of a diagnostic reagent of the second type, is indicative of the
21 presence of the glycosylation disorder in the mammal.
- 1 2. The method of claim 1, wherein the glycoconjugates are associated with
2 a cell.
- 1 3. The method of claim 1, wherein the glycoconjugates are selected from
2 the group consisting of glycoproteins, glycolipids, and proteoglycans.
- 1 4. The method of claim 1, wherein the sample is contacted with two or
2 more different diagnostic reagents.

1 5. The method of claim 4, wherein at least one of the diagnostic reagents is
2 of the first type and at least one of the diagnostic reagents is of the second type.

1 6. The method of claim 4, wherein each of the different diagnostic
2 reagents comprises a different label.

1 7. The method of claim 1, wherein the diagnostic reagent specifically
2 binds to the oligosaccharide determinant, if the oligosaccharide determinant is present in the
3 sample.

1 8. The method of claim 7, wherein the diagnostic reagents comprise a
2 binding component that is selected from the group consisting of a lectin, an antibody, and an
3 acceptor binding moiety of a glycosyltransferase.

1 9. The method of claim 1, wherein sample is contacted with a diagnostic
2 reagent of the first type that binds to a polypeptide that, due to the glycosylation disorder,
3 lacks an oligosaccharide determinant that would otherwise be attached to a particular amino
4 acid of the polypeptide, but which does not bind to the polypeptide when the polypeptide has
5 the oligosaccharide determinant attached at this amino acid.

1 10. The method of claim 9, wherein the absence of the oligosaccharide
2 determinant causes a conformational change in the polypeptide or unmasks a binding site for
3 the diagnostic reagent.

1 11. The method of claim 9, wherein the polypeptide is transferrin.

1 12. The method of claim 11, wherein the amino acid is selected from the
2 group consisting of N432 and N630.

1 13. The method of claim 9, wherein the glycosylation disorder is
2 alcoholism.

1 14. The method of claim 9, wherein the diagnostic reagent comprises a
2 binding component that comprises an antibody or a binding fragment thereof.

1 15. The method of claim 1, wherein sample is contacted with a diagnostic
2 reagent of the second type that does not bind to a polypeptide that, due to the glycosylation
3 disorder, lacks an oligosaccharide determinant that would otherwise be attached to a
4 particular amino acid of the polypeptide, but which does bind to the polypeptide when the
5 polypeptide has the oligosaccharide determinant attached at this amino acid.

1 16. The method of claim 15, wherein the diagnostic reagent comprises a
2 binding component that comprises an antibody or a binding fragment thereof.

1 17. The method of claim 1, wherein the glycosylation disorder is Congenital
2 Dyserythropoietic Anemia Type II.

1 18. The method of claim 17, wherein the sample comprises whole blood
2 from the mammal and the presence of the glycosylation disorder is associated with reduced
3 binding of a detection reagent which comprises E-PHA.

1 19. The method of claim 17, wherein the sample comprises whole blood
2 from the mammal and the presence of the glycosylation disorder is associated with increased
3 binding of a detection reagent which comprises tomato lectin.

1 20. The method of claim 1, wherein the glycosylation disorder is
2 Carbohydrate Deficient Glycoprotein Syndrome Type II.

1 21. The method of claim 20, wherein:
2 the sample comprises blood, plasma, or serum from the mammal and
3 the presence of the glycosylation disorder is associated with reduced binding of a detection
4 reagent which comprises E-PHA lectin; or

5 the sample comprises blood of the mammal and the presence of the
6 glycosylation disorder is associated with reduced binding of a detection reagent which
7 comprises L-PHA lectin.

1 22. The method of claim 20, wherein the sample comprises blood of the
2 mammal and the presence of the glycosylation disorder is associated with increased binding
3 of a detection reagent which comprises ConA lectin.

1 23. The method of claim 1, wherein the glycosylation disorder is associated
2 with alcoholism.

1 24. A method of monitoring the course of treatment of a glycosylation
2 disorder in a mammal, the method comprising:
3 obtaining a first sample which comprises a plurality of glycoconjugates
4 from the mammal;
5 administering to the mammal a potential treatment regime for the
6 glycosylation disorder;
7 obtaining at least a second sample which comprises a plurality of
8 glycoconjugates from the mammal; and
9 contacting the first sample and the second sample with a diagnostic
10 reagent and determining whether the amount of diagnostic reagent binding to the second
11 sample is increased or decreased compared to amount of diagnostic reagent binding to the
12 first sample;

13 wherein the diagnostic reagent is selected from the group consisting of:
14 a first type of diagnostic reagent that binds to a glycoconjugate
15 that has an oligosaccharide determinant that: i) is present on
16 glycoconjugates in a sample obtained from a mammal that has the
17 glycosylation disorder, and ii) is not present on glycoconjugates in a
18 sample obtained from a mammal that does not have the
19 glycosylation disorder; and
20 a second type of diagnostic reagent that binds to a
21 glycoconjugate that has an oligosaccharide determinant that is: i) is

22 present on glycoconjugates in a sample obtained from a mammal
23 that does not have the glycosylation disorder, and ii) is not present
24 on glycoconjugates in a sample obtained from a mammal that has
25 the glycosylation disorder; and
26 an effective treatment regime is indicated by decreased binding of a
27 diagnostic reagent of the first type, or by increased binding of a diagnostic reagent of the
28 second type, to the second sample relative to the first sample.

1 25. The method of claim 24, wherein the first sample is obtained after an
2 initial administration of a potential treatment regime to the mammal.

1 26. A method of detecting a genetically transmitted immune system
2 dysfunction in a mammal, wherein the dysfunction is associated with a glycosylation
3 disorder, the method comprising:

4 a) providing a sample from a mammal, wherein the sample comprises
5 a plurality of glycoconjugates;

6 b) contacting the sample with either or both of:

7 a first type of diagnostic reagent that binds to a glycoconjugate
8 that has an oligosaccharide determinant that: i) is present on
9 glycoconjugates in a sample obtained from a mammal that has the
10 immune system dysfunction, and ii) is not present on
11 glycoconjugates in a sample obtained from a mammal that does not
12 have the immune system dysfunction; and

13 a second type of diagnostic reagent that binds to a
14 glycoconjugate that has an oligosaccharide determinant that is: i) is
15 present on glycoconjugates in a sample obtained from a mammal
16 that does not have the immune system dysfunction, and ii) is not
17 present on glycoconjugates in a sample obtained from a mammal
18 that has the immune system dysfunction; and

19 c) determining whether the diagnostic reagent binds to the
20 glycoconjugates in the sample, wherein the binding of a diagnostic reagent of the first type,

21 or the absence of binding of a diagnostic reagent of the second type, is indicative of the
22 presence of the immune system dysfunction in the mammal.

1 27. The method of claim 26, wherein the immune system dysfunction is B
2 lymphocyte dysfunction.

1 28. The method of claim 27, wherein the presence of the immune system
2 dysfunction is associated with reduced binding to a detection reagent which comprises SNA
3 or CD22.

1 29. The method of claim 28, wherein the detection reagent comprises
2 CD22-Ig.

1 30. The method of claim 26, wherein the immune system dysfunction is
2 cytotoxic T cell deficiency.

1 31. The method of claim 30, wherein the presence of the immune system
2 dysfunction is associated with increased binding of a detection reagent which specifically
3 binds to Gal β 1-3GalNAc but does not bind to Sia α 2-3Gal β 1-3GalNAc.

1 32. The method of claim 31, wherein the detection reagent comprises PNA
2 lectin or Jacalin.

1 33. The method of claim 30, wherein the presence of the immune system
2 dysfunction is associated with reduced binding of a detection reagent which specifically
3 binds to α 2-3-linked sialic acids.

1 34. The method of claim 33, wherein the detection reagent comprises a
2 MAL II lectin.

1 35. The method of claim 26, wherein the immune system dysfunction is
2 myeloid deficiency.

1 36. The method of claim 35, wherein the presence of the immune system
2 dysfunction is associated with reduced binding to a detection reagent which specifically
3 binds to Core 2 type O-glycans.

1 37. The method of claim 36, wherein the detection reagent comprises an
2 antibody selected from the group consisting of B220 and 1B11.

1 38. A chimeric or transgenic nonhuman mammal which comprises cells
2 having a defect in a gene which encodes an enzyme involved in biosynthesis of an
3 oligosaccharide determinant of a glycoconjugate.

1 39. The chimeric or transgenic mammal of claim 38, wherein the defect
2 reduces or prevents expression of the enzyme.

1 40. The chimeric or transgenic mammal of claim 38, wherein the mammal
2 is a mouse.

1 41. The chimeric or transgenic mammal of claim 38, wherein the defect
2 results in expression of an enzyme having substantially reduced activity compared to an
3 enzyme encoded by a gene which lacks the defect.

1 42. The chimeric or transgenic mammal of claim 38, wherein the enzyme is
2 selected from the group consisting of an oligosaccharyltransferase, an α -glucosidase I, an α -
3 glucosidase II, an ER α 1,2-mannosidase, an *N*-acetylglucosaminyl-phosphotransferase, an
4 *N*-acetylglucosamine-1-phosphodiester α -*N*-acetylglucosaminidase, a Golgi α -mannosidase
5 I, an *N*-acetylglucosaminyltransferase I, a Golgi α -mannosidase II, an *N*-
6 acetylglucosaminyltransferase II, a fucosyltransferase, a galactosyltransferase, and a
7 glucosyltransferase.

1 43. The chimeric or transgenic mammal of claim 38, wherein the gene is
2 selected from the group consisting of:

3 an *MGAT2* gene, wherein the mammal exhibits symptoms of CDGS
4 Type II;
5 an ST6Gal sialyltransferase gene, wherein the mammal exhibits
6 symptoms of an immunodeficiency characterized by a defect in a B lymphocyte-mediated
7 immune response;
8 an ST3Gal I sialyltransferase gene, wherein the mammal exhibits
9 symptoms of an immunodeficiency characterized by a defect in a cytotoxic T lymphocyte-
10 mediated immune response.

1 44. The chimeric or transgenic mammal of claim 43, wherein the mammal
2 has a defective *MGAT2* gene and exhibits symptoms of Carbohydrate Deficient Glycoprotein
3 Syndrome Type II.

1 45. The chimeric or transgenic mammal of claim 43, wherein the mammal
2 has a defective ST6Gal sialyltransferase gene and exhibits B lymphocyte dysfunction.

1 46. The chimeric or transgenic mammal of claim 43, wherein the mammal
2 has a defective Core 2 GlcNAc-transferase gene and exhibits myeloid insufficiency.

1 47. The chimeric or transgenic mammal of claim 43, wherein the mammal
2 has a defective ST3Gal I sialyltransferase gene and exhibits CTL immunodeficiency.

1 48. A kit for use in diagnosing a glycosylation disorder in a mammal, the kit
2 comprising a diagnostic reagent selected from the group consisting of:
3 a first type of diagnostic reagent that binds to a glycoconjugate that has
4 an oligosaccharide determinant that: i) is present on glycoconjugates in a sample obtained
5 from a mammal that has the glycosylation disorder, and ii) is not present on glycoconjugates
6 in a sample obtained from a mammal that does not have the glycosylation disorder; and
7 a second type of diagnostic reagent that binds to a glycoconjugate that
8 has an oligosaccharide determinant that is: i) is present on glycoconjugates in a sample
9 obtained from a mammal that does not have the glycosylation disorder, and ii) is not present
10 on glycoconjugates in a sample obtained from a mammal that has the glycosylation disorder.

1 **51.** The kit of claim 48, wherein the kit comprises a panel of diagnostic
2 reagents.

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